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USARIEM TECHNICAL REPORT T03-11

**INFLUENCE OF MODERATE ALTITUDE RESIDENCE ON
ARTERIAL OXYGEN SATURATION AT HIGHER ALTITUDES**

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DISCLAIMER

The investigators have adhered to the policies for protection of human subjects as prescribed in Army Regulation 70-25, and the research was conducted in adherence with the provisions of 45 CFR Part 46

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BACKGROUND

Mountainous terrain provides sanctuary for hostile forces as seen in Central and West Asia, the Balkans, and South America. This harsh environment lessens U.S. military technological superiority by limiting use of air support and crew-served combat vehicles. This places the burden of combat on dismounted warfighters. Objective Force Warrior (OFW) emphasizes the rapid deployment and mobility of troops to conduct operations for sustained periods without relief. However, rapid deployment of unacclimatized troops to high mountainous environments causes debilitating effects on fighting capabilities and Force health. Environmental illnesses are a significant portion of the non-battle injuries sustained by U.S. military forces. For example, during a major combat operation in Afghanistan, ~12% of medevacs and hospital admissions were due to severe Acute Mountain Sickness. Available guidance for minimizing adverse effects of high altitude is based on worst-case scenarios that assume the personnel have no degree of altitude acclimatization. Many military bases are located at altitudes at which personnel will develop some magnitude of altitude acclimatization (>1,500 m). However, the magnitude of altitude acclimatization developed in lowlanders residing at moderate altitudes has not been well documented. This study compared the distribution of arterial oxygen saturation and subjective symptoms to hypoxia in moderate altitude residents and low altitude residents following rapid ascent to 4,056 m (pressure altitude). This work will add to a database that will contribute to the development of models that should provide operational commanders with medical planning capability for high mountainous operations, resulting in decreased altitude illness, and reduced manpower and logistical and medical support requirements.

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EXECUTIVE SUMMARY

The magnitude of altitude acclimatization developed in lowlanders residing at moderate elevations (1,000 - 2,000 m) has not been well documented. Moreover, there is no comprehensive database that describes the degree to which acclimatization to moderate altitudes improves arterial oxygenation upon rapid ascent to altitudes above 2,000 m. We propose that lowlanders acclimatized to moderate altitudes will maintain a higher level of arterial oxygenation when rapidly ascending to higher altitudes compared to lowlanders residing at low altitudes.

The purpose of this study was to compare the distribution of arterial oxygen saturation (SaO_2) and subjective symptoms to hypoxia in moderate altitude residents (MAR) and low altitude residents (LAR) following rapid ascent to 4,056 m (pressure altitude). Resting ventilatory parameters (open-circuit spirometry) and SaO_2 (pulse oximetry) were measured in 38 volunteers (25 men, 13 women) residing for >3 months near Colorado Springs, CO (MAR group). These measurements were made at 1,940 m (US Air Force Academy) and after ~1 h at 4,056 m on the summit of Pikes Peak, CO, following ascent by car. Resting SaO_2 was also measured at 610 m elevation intervals during the ascent. The 39 (30 men, 9 women) LAR volunteers were exposed to a similar ascent profile in a hypobaric chamber.

The following results were obtained ($\bar{X} \pm \text{S.D.}$): At 1,940 m the MAR group PETCO_2 and SaO_2 were 33.6 ± 2.8 mmHg and $94 \pm 1\%$, respectively, and decreased ($p<0.001$) to 32.1 ± 4.5 mmHg and $86 \pm 2\%$ at 4,056 m. At 50 m the LAR group PETCO_2 and SaO_2 were 38.7 ± 2.7 mmHg and $98 \pm 1\%$, respectively, and decreased ($p<0.001$) to 36.4 ± 3.5 mmHg and $82 \pm 5\%$ at 4,056 m. Above 2,438 m to 4,056 m, the MAR group SaO_2 was higher ($p<0.001$) than the LAR group. For all subjects, the PETCO_2 at their residence altitudes showed an indirect correlation to PETO_2 and SaO_2 and a direct correlation to PETCO_2 at 4,056 m. Only 1 of the MAR but 9 of the LAR subjects reported symptoms of Acute Mountain Sickness (AMS).

When referenced to published acclimatization data (13,14), our results suggest that prolonged residence at ~2,000 m elevation induces a level of ventilatory acclimatization equivalent to residing at 4,056 m for approximately 5 - 9 days. We speculate that given the degree of ventilatory acclimatization achieved by personnel residing at the moderate altitude studied, we would expect such personnel to be less susceptible to AMS and decrements in cognitive and physical performance during rapid ascent to higher altitudes.

INTRODUCTION

During long-term (days to weeks) exposures to high altitudes, humans compensate for the decreased inspired oxygen partial pressure (PiO_2) by progressively increasing ventilation (for a review, see references (5,25)). For example, following rapid ascent to 4,300 m elevation, ventilation increases during the first 6 - 8 days (14). The rise in ventilation produces a decrease in arterial carbon dioxide partial pressure (PaCO_2) and a concomitant increase in PaO_2 (23).

The time course and magnitude for acquiring altitude acclimatization has been well described for unacclimatized lowlanders rapidly ascending to high altitudes. However, the magnitude of altitude acclimatization developed in lowlanders residing at moderate elevations (1,000 - 2,000 m) has not been well documented. Moreover, there is no comprehensive database that describes the degree to which acclimatization to moderate altitudes improves arterial oxygenation upon rapid ascent to altitudes above 2,000 m. We propose that lowlanders acclimatized to moderate altitudes will maintain a higher level of arterial oxygenation when rapidly ascending to higher altitudes compared to lowlanders residing at low altitudes.

Numerous military installations housing large numbers of military personnel are located at moderate altitudes. Development of a database that describes the distribution of arterial oxygen saturation in lowlanders acclimatized to a range of moderate altitudes would provide commanders with ascent timetables to higher elevations that take full advantage of the personnel's acclimatization status. Furthermore, current limits on the time that aircrews of unpressurized aircraft may fly above 3,048 m without supplemental oxygen are based on studies of unacclimatized lowlanders. Altitude-acclimatized aircrews may be able to safely operate beyond these limits, thus enhancing operational capability.

The purpose of this study was to determine the distribution of resting arterial oxygen saturation in personnel residing near sea level or acclimatized to moderate (1,675 - 2,255 m) altitude following rapid ascent to altitudes between 1,940 and 4,056 m. To determine if acclimatization to moderate altitude improves arterial oxygen saturation at higher altitudes, comparisons were made between personnel acclimatized to moderate altitude and unacclimatized subjects.

METHODS

Studies were conducted on 77 military personnel divided into two groups based on their residence altitude (Table 1). The low altitude residents (LAR) resided near sea level (elevation 20 - 100 m) in the Boston, MA, metropolitan area. The LAR group volunteers were military personnel assigned to SSCOM or ARIEM in Natick, MA. The moderate altitude residents (MAR) resided in the Colorado Springs, CO, metropolitan area (elevation ranging from 1,675 - 2,255 m). The MAR group consisted of military personnel assigned to the U.S. Air Force Academy (USAFA) or Pederson AFB, CO.

Personnel in each group had resided at their respective elevation for at least 3 months prior to the study. All the subjects had passed their most recent military physical performance test and were in good health. Women volunteers tested negative for pregnancy.

Table 1. LAR and MAR subject characteristics.

Group	N	# males	# females	Age (y)	Height (cm)	Weight (kg)
MAR	38	25	13	$34.8 \pm 7.8^*$	175.5 ± 8.5	74.9 ± 13.8
LAR	39	30	9	26.2 ± 8.8	175.4 ± 9.9	77.5 ± 12.9

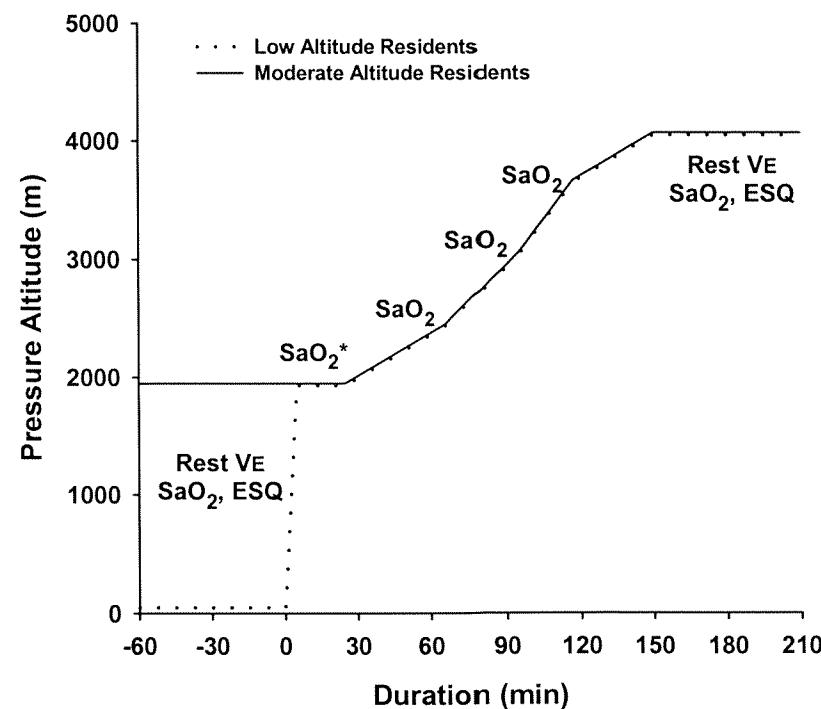
$\bar{X} \pm S.D.$ * $p < 0.05$ MAR vs. LAR

The MAR group was studied first. For each subject, all testing was completed on 1 day. On the day of testing, subjects reported to an indoor test site located at the USAFA ($Pb 606 \pm 1$ mmHg, pressure altitude 1,940 m). At that site, several test procedures were performed: administration of an Environmental Background Survey (EBS) and the Environmental Symptoms Questionnaire (ESQ), and measurement of resting ventilatory parameters.

After completion of these procedures, subjects entered a van and were transported to the U.S. Army Pikes Peak Laboratory Facility on the summit (4,300 m terrestrial elevation) of Pikes Peak, CO, via the Pikes Peak Highway. The van stopped at the following pressure altitudes according to the prevailing barometric pressure: 2,438 m ($Pb 560 \pm 2$ mmHg), 3,048 m ($Pb 521 \pm 1$ mmHg), 3,658 m ($Pb 484 \pm 1$ mmHg) and 4,056 m ($Pb 459 \pm 1$ mmHg). At each stop, the subjects remained in the van at rest for approximately 5 min after which their arterial oxygen saturation (SaO_2) and heart rate (HR) were recorded. Upon arriving at the summit, the same 5 min measurements were made after which the subjects entered the U.S. Army Pikes Peak Laboratory Facility. The subject's resting ventilatory parameters were measured within 50 min of arriving on the summit. After about 1 h on the summit, the subjects were administered the ESQ. The subjects then returned to the USAFA and were released from the study. The ascent profile is illustrated in Figure 1.

The LAR group was tested at the USARIEM hypobaric chamber facility, Natick, MA. The same test order and procedures previously performed on the MAR group were followed. Baseline measurements were made at the prevailing barometric pressure (759 ± 8 mmHg). Then the hypobaric chamber was decompressed at 305 m/min to a pressure altitude of 1,940 m (equivalent to the MAR baseline test altitude). After 20 minutes at this altitude, resting SaO_2 and HR were recorded. Then the same average ascent rate to higher altitudes previously obtained during the MAR group tests (Figure 1) was duplicated in the hypobaric chamber.

Figure 1. Ascent profile for the LAR and MAR group subjects starting from each group's respective residence altitude.



At both test sites the following test procedures were performed. Each subject's height and weight were measured. Then each subject completed the EBS. The EBS is a 57-item questionnaire designed to elicit information on test volunteer's previous experience in stressful climatic conditions, participation in physical activities, and medical history. The presence of hypoxic-induced symptoms (dizziness, shortness of breath, alertness, etc) and the incidence of Acute Mountain Sickness (AMS) were determined from information gathered using the ESQ. The ESQ is a self-reported, 67-question inventory used to document symptoms induced by altitude and other stressful environments (19). A weighted average of scores from cerebral symptoms (headache, lightheaded, dizzy, etc.) designated AMS-C and from respiratory symptoms (short-of-breath, hurts-to-breathe, etc.) designated AMS-R were calculated. AMS-C scores greater than 0.7 and AMS-R scores greater than 0.6 are defined as indicating the presence of AMS (19). Also, an alertness factor and fatigue factor were calculated from the questionnaire (19).

Each subject's resting minute ventilation (VE), and end-tidal oxygen and carbon dioxide partial pressure (P_{ETCO_2} and P_{ETO_2}) were measured using an open-circuit metabolic measurement system (SensorMedics Vmax229). Simultaneously, SaO_2 and HR were measured by pulse oximetry (Nellcor N-200). The subjects were studied after having fasted for at least 2 h and having been seated at rest for at least 10 min. Resting ventilation was measured once at the subject's residence altitude (1,940 m for the MAR group and 50 m for the LAR group), and once upon arrival on the summit of

Pikes Peak (MAR group) or the same equivalent pressure altitude in the hypobaric chamber (LAR group).

STATISTICAL ANALYSIS

To determine if acclimatization to moderate altitude improves arterial oxygen saturation at higher altitudes, two-way (residence altitude group and altitude exposure) analysis of variance with repeated measures in one factor (altitude exposure) was used to analyze the data. Data that deviated significantly from normality or failed to meet the qualifying assumptions of analysis of variance were analyzed using appropriate non-parametric techniques (i.e., ANOVA on ranks, or Mann-Whitney rank sum test). Possible gender influences were analyzed using the T-test, or if the data deviated significantly from normality or failed to meet the qualifying assumptions of analysis of variance, the data were analyzed using the Mann-Whitney Rank Sum Test. Lastly, potential relationships between measured parameters were tested using the Pearson Product Moment Correlation. Statistical significance was accepted at $p \leq 0.05$. All data are reported as the group mean (\bar{X}) \pm standard deviation (S.D.).

RESULTS

Subject demographics are presented in Table 1. Based on analysis of the EBS, all subjects regularly participated in aerobic physical conditioning and nearly half in strength conditioning. The MAR were significantly older than the LAR.

MAR GROUP RESULTS

Resting ventilatory parameters are listed in Table 2. At the MAR test site, PETO_2 , PETCO_2 , and SaO_2 were significantly ($p < 0.05$) lower than normal values reported for lowlanders residing near sea level (7). During the approximately 2 h ascent to 4,056 m, resting SaO_2 progressively decreased (Table 3). The decrease in SaO_2 with increasing altitude was significant ($p < 0.001$) at and above the 3,048 m elevation. There was no significant change in resting HR (Table 3) during the ascent to 4,056 m.

Table 2. Resting ventilatory parameters at residence altitudes and following rapid ascent to high altitude for the LAR and MAR subjects.

Group	Altitude (m)	VO ₂ (l/min)	VE (l/min)	PETO ₂ (mmHg)	PETCO ₂ (mmHg)	SaO ₂ (%)	HR (b/m)
MAR	1,940	0.296 ± 0.051	10.7 ± 2.3	75.4 ± 4.9 *	33.6 ± 2.8 *	94 ± 1 *	71 ± 11
	4,056	0.284 ± 0.053	10.5 ± 2.6	51.5 ± 5.7 †	32.1 ± 4.5 *	87 ± 3 *†	68 ± 9
LAR	50	0.222 ± 0.064	10.3 ± 1.8	105.9 ± 3.4	38.7 ± 2.7	98 ± 1	73 ± 10
	4,056	0.249 ± 0.072	12.1 ± 2.5	48.0 ± 4.1 †	36.4 ± 3.5 †	82 ± 5 †	83 ± 13 †

$\bar{X} \pm S.D.$ * p<0.05 Residence altitude vs. 4,056 m. * p<0.05 MAR vs. LAR

Table 3. Resting SaO₂ and HR following rapid ascent to moderate and high altitudes for the LAR and MAR subjects.

Pressure Altitude (m)	MAR GROUP		LAR GROUP	
	SaO ₂ (%)	HR (b/m)	SaO ₂ (%)	HR (b/m)
1,940	94 ± 1	71 ± 11	96 ± 2	70 ± 8
2,438	94 ± 2	68 ± 9	94 ± 2	73 ± 10
3,048	92 ± 2	68 ± 8	91 ± 2	75 ± 11
3,658	90 ± 2 *	68 ± 8 *	86 ± 3	78 ± 12
4,056	87 ± 3 *	68 ± 9 *	82 ± 5	83 ± 13

$\bar{X} \pm S.D.$ * p<0.05 MAR vs. LAR

The SaO₂, PETO₂ and PETCO₂ decreased significantly between 1,940 m and 4,056 m in all MAR subjects (Table 2), but there was no change in resting metabolic rate (VO₂). The SaO₂ showed an 8% mean decrease between 1,940 m and 4,056 m. The range of SaO₂ at 4,056 m was 83%-93%. At 1,940 m, ventilation in the MAR group females was significantly greater than in the males (Table 4), but there was no significant difference in these values between MAR group males and females at 4,056 m. Interindividual differences in resting SaO₂ at 4,056 m were not related to age, physical fitness, or frequency of trips to altitudes above 1,940 m. For all MAR subjects, the PETCO₂ at their residence altitude (1,940 m) showed an indirect correlation to SaO₂ and a direct correlation to PETCO₂ at 4,056 m (Table 5). Likewise, the MAR subjects resting SaO₂ at 2,438 m was positively correlated with their resting SaO₂ at each higher altitude (Table 6).

Table 4. Between-gender comparison of resting ventilatory parameters at residence altitudes and following rapid ascent to high altitude for the LAR and MAR subjects.

Group	Altitude (m)	Males			Females		
		P _{ETCO₂} (mmHg)	P _{ETO₂} (mmHg)	SaO ₂ (%)	P _{ETCO₂} (mmHg)	P _{ETO₂} (mmHg)	SaO ₂ (%)
MAR	1,940	34.2 ± 2.8	74.0 ± 4.9	94 ± 1	32.3 ± 2.1 [†]	78.1 ± 3.7 [†]	95 ± 1
	4,056	32.7 ± 4.1	50.9 ± 4.5	86 ± 2	30.9 ± 5.0	52.8 ± 7.6	86 ± 3
LAR	50	39.3 ± 2.6	105.2 ± 3.4	98 ± 1	36.9 ± 2.2 [†]	108.2 ± 2.1 [†]	99 ± 1
	4,056	36.6 ± 3.8	47.5 ± 4.1	82 ± 5	35.8 ± 2.4	49.8 ± 3.5	84 ± 6

$\bar{X} \pm S.D.$ [†]p<0.05 Females vs. Males within MAR and LAR groups.

Table 5. Correlation coefficients (r) between resting P_{ETCO₂} at residence altitudes and resting P_{ETCO₂}, P_{ETO₂} and SaO₂ at 4,056 m for the LAR and MAR subjects.

Group	N	4,056 m P _{ETCO₂}		4,056 m P _{ETO₂}		4,056 m SaO ₂	
		r	P	R	P	r	P
MAR	38	0.80	>0.0001	-0.66	>0.0001	-0.42	0.013
LAR	39	0.56	0.0002	-0.40	0.011	-0.23	0.17

Table 6. Correlation coefficients (r) between resting SaO₂ at select altitudes and resting SaO₂ at higher altitudes for the LAR and MAR subjects.

Group	SaO ₂	3,048 m	3,658 m	4,056 m
MAR	2,438 m	0.65*	0.40*	0.30
	3,048 m	-	0.56*	0.51*
	3,658 m		-	0.78*
LAR	2,438 m	0.50*	0.58*	0.36*
	3,048 m	-	0.63*	0.64*
	3,658 m		-	0.54*

* p<0.05

Although there were significant ($p<0.001$) increases in both AMS-C and AMS-R scores at 4,056 m, only one MAR subject's AMS-C score met the diagnostic criterion for AMS. The mean AMS-C and AMS-R scores were well below the 0.7 and 0.6 threshold criterion for AMS (site article) (Table 7). Compared to 1,940 m, fatigue scores showed a small but significant increase ($p<0.001$) at 4,056 m. However, alertness was not affected by ascent to 4,056 m.

Table 7. The LAR and MAR subjects' symptom scores at 4,056 m altitude following rapid ascent.

Group	Altitude (m)	AMS-C	AMS-R	Alertness	Fatigue
MAR	1,940	0.020 ± 0.050	0.075 ± 0.105	1.791 ± 0.809	0.165 ± 0.187
	4,056	$0.291 \pm 0.194^{\dagger}$	$0.135 \pm 0.135^{\dagger}$	1.893 ± 0.534	$0.502 \pm 0.378^{\dagger}$
LAR	50	0.014 ± 0.041	0.082 ± 0.104	1.809 ± 0.828	0.215 ± 0.222
	4,056	$0.360 \pm 0.363^{\dagger}$	$0.301 \pm 0.263^{\dagger}$	1.714 ± 0.756	$0.703 \pm 0.489^{\dagger*}$

$\bar{X} \pm S.D.$ $^{\dagger} p<0.05$ Residence altitude vs. 4,056 m. $^{*} p<0.05$ MAR vs. LAR

LAR GROUP RESULTS

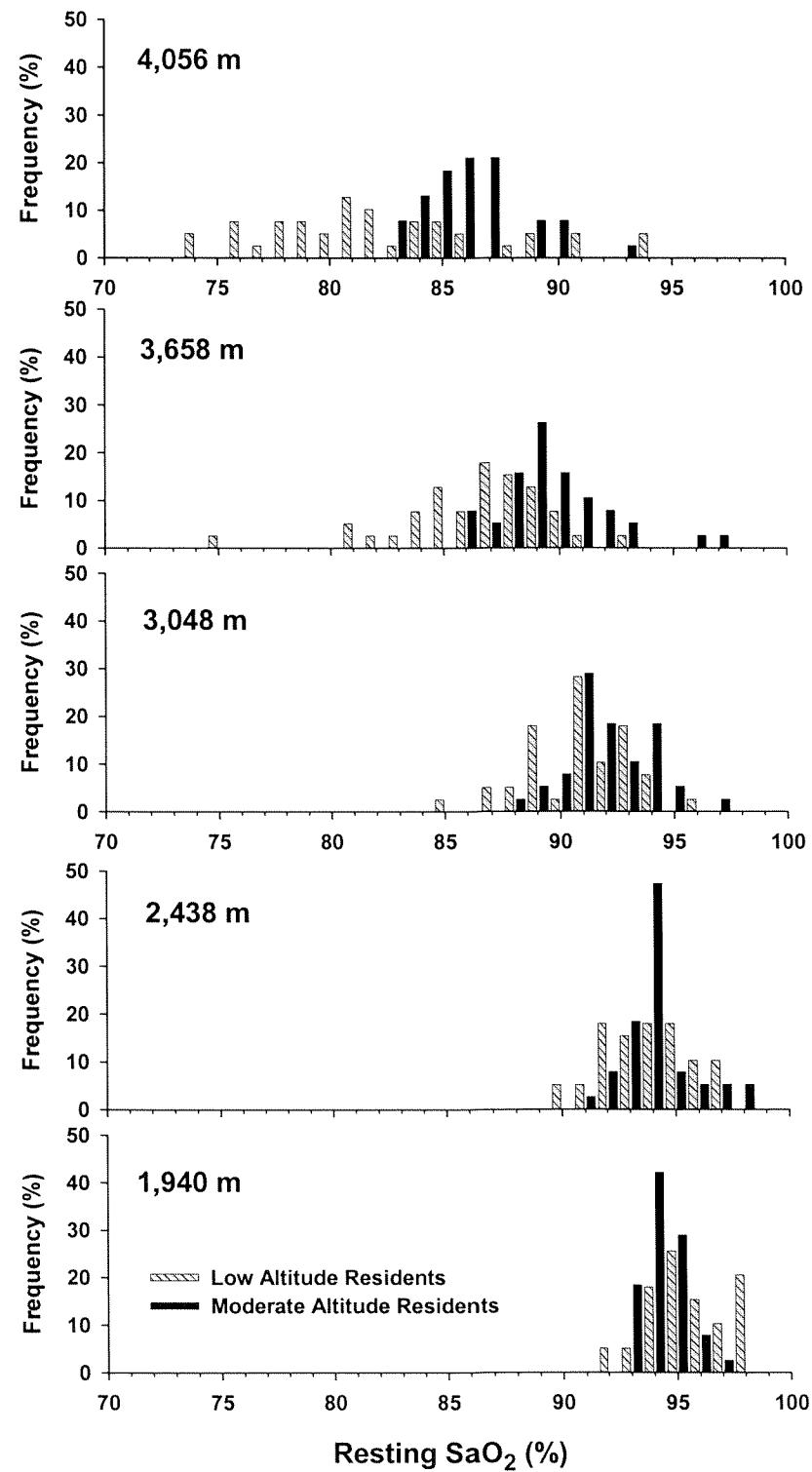
At the LAR test site (50 m), resting SaO_2 , $PETO_2$ and $PETCO_2$ were within the normal range for unacclimatized lowlanders (7). These values decreased significantly during ascent to 4,056 m, but there was no change in resting metabolic rate. Specifically, the decrease in SaO_2 with increasing altitude was significant ($p<0.001$) at and above 1,940 m elevation. The SaO_2 showed a $16 \pm 5\%$ decrease between 50 m and 4,056 m. The range of SaO_2 at 4,056 m was 74%-96%. At 50 m altitude, ventilation in the LAR group females was significantly greater than in the males (Table 4), but there was no significant difference between males and females SaO_2 at or above 1,940 m, nor $PETCO_2$ or $PETO_2$ at 4,056 m (Table 4). Furthermore, interindividual differences in resting SaO_2 at 4,056 m were not related to age, physical fitness or frequency of trips to higher altitudes. For all LAR subjects, the $PETCO_2$ at their residence altitude (~50 m) showed a direct correlation to $PETCO_2$ at 4,056 m and an indirect correlation to $PETO_2$ but not SaO_2 at 4,056 m (Table 5). Likewise, the LAR subjects resting SaO_2 at 2,438 m was positively correlated with their resting SaO_2 at each higher altitude (Table 6).

In the LAR group, there were significant ($p<0.001$) increases in both AMS-C and AMS-R scores at 4,056 m (Table 7). Although the mean AMS-C and AMS-R scores were well below the 0.7 and 0.6 threshold criterion for AMS, the AMS-C scores of 9 subjects in the LAR group met the criteria for diagnosis of AMS. There was no correlation between AMS symptom scores and resting ventilation parameters at 4,056 m. Compared to 50 m, fatigue scores showed a small but significant increase at 4,056 m. However, alertness was not affected by ascent to 4,056 m.

COMPARISON BETWEEN MAR & LAR

At 1,940 m the MAR group PETO₂, PETCO₂, and SaO₂ were lower ($p<0.001$) than the sea level values obtained from the LAR subjects (Table 2). After the LAR subjects were decompressed to 1,940 m in the hypobaric chamber, their SaO₂ values were not significantly different from the MAR group at that altitude (Table 3) or at 2,438 m. However, with further ascent above 2,438 m, the MAR group resting SaO₂ was significantly greater than the LAR group resting SaO₂ at all higher altitudes. Ultimately, the mean difference in SaO₂ between the two groups increased to 5% with ascent to 4,056 m. The distribution of resting SaO₂ for both groups at altitudes between 1,940 to 4,056 m is illustrated in Figure 2. In addition to the shift to lower resting SaO₂ in both groups with increasing altitude, these frequency distribution histograms clearly show that the range of resting SaO₂ widened more in the LAR group than in the MAR group at all altitudes.

Figure 2. Frequency distribution histograms of resting SaO_2 for both MAR and LAR groups at altitudes between 1,940 to 4,056 m.



At 4,056 m, the greater ventilation in the MAR group compared to the LAR group is substantiated by the MAR group higher PETO₂ and lower PETCO₂ (Table 2). Figure 3 shows the frequency distribution of resting PETCO₂ for both groups at their residence altitudes and 4,056 m. At both altitudes, the MAR group range of resting PETCO₂ was shifted to lower values relative to the LAR group. When the two groups' resting PETCO₂ values were combined, the wide range of individual resting PETCO₂ values yield significant direct correlation between residence altitude PETCO₂ and their PETCO₂ at 4,056 m and an indirect correlation to SaO₂ at 4,056 m (Figure 4).

Figure 3. Frequency distribution histograms of resting PETCO₂ for both MAR and LAR groups at their respective residence altitudes and 4,056 m.

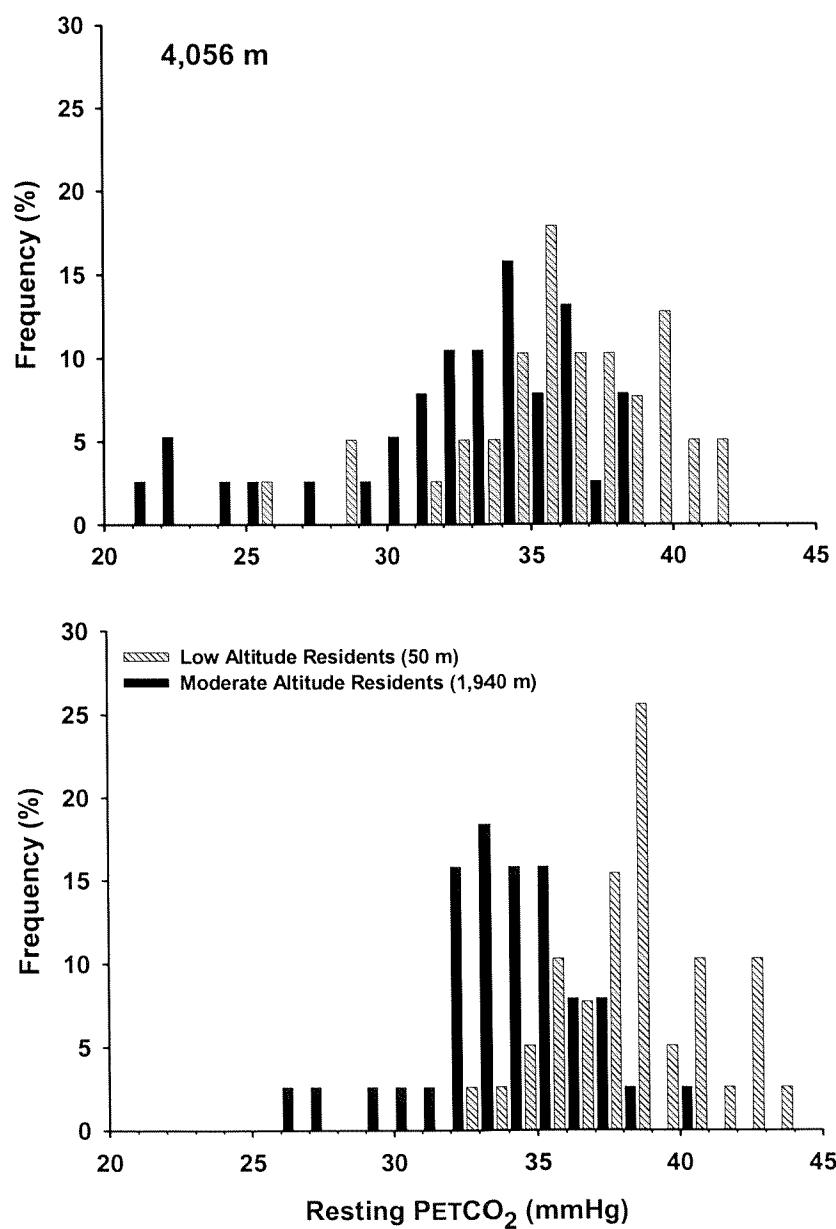
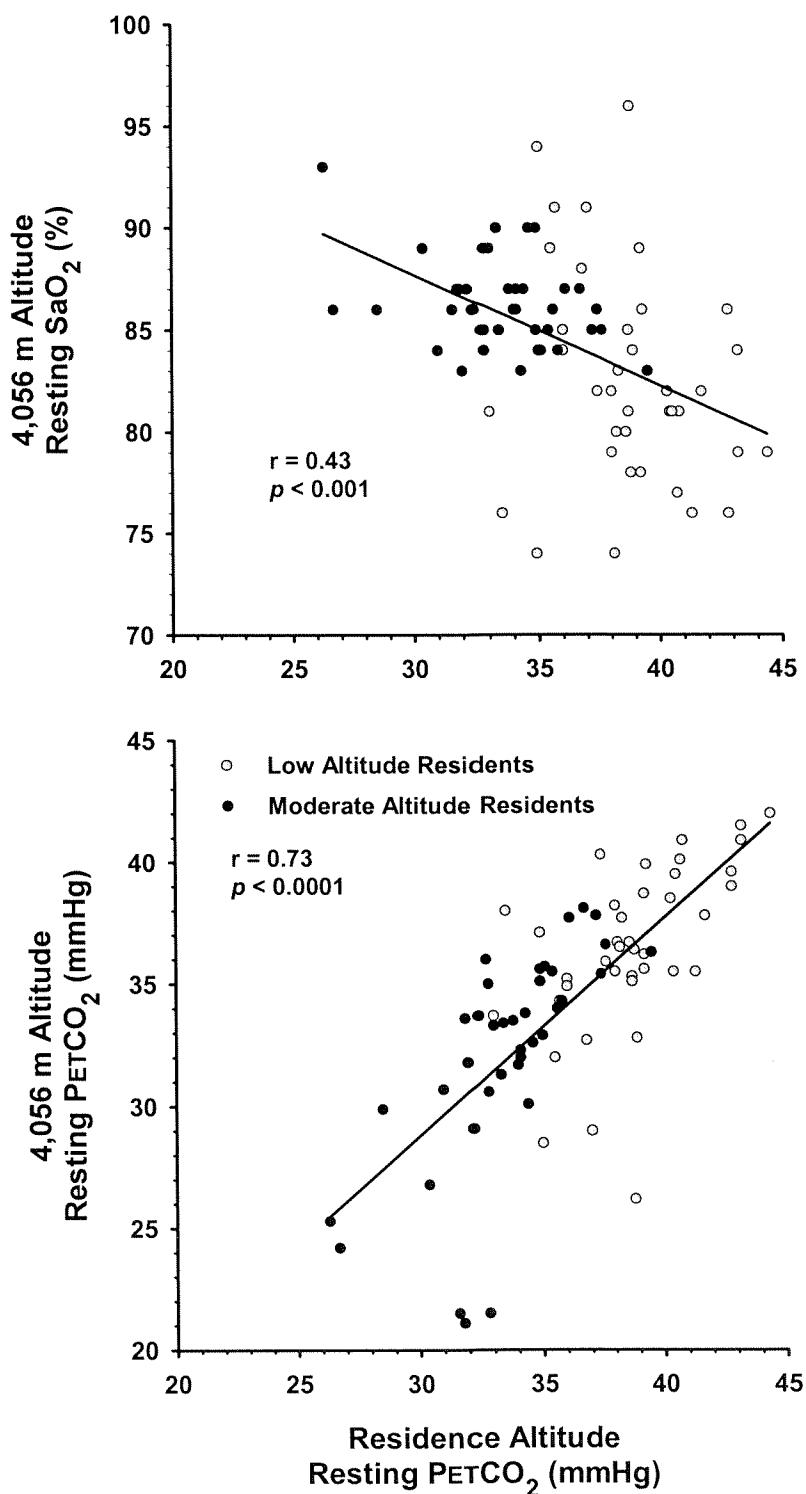
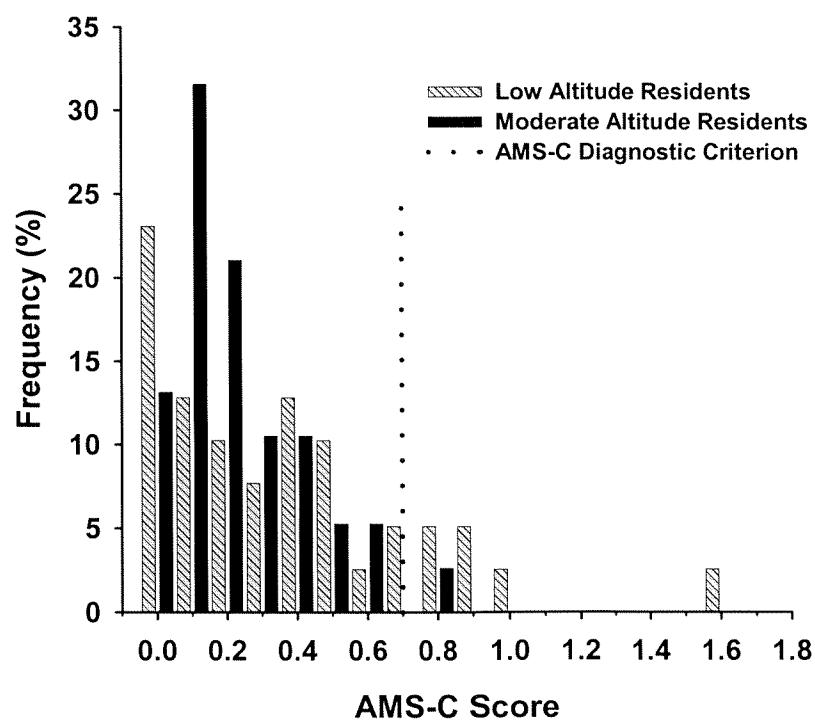


Figure 4. Correlations between residence altitude resting PETCO₂ and resting PETCO₂ and SaO₂ at 4,056 m for all subjects (MAR and LAR groups combined).



The mean AMS-C and AMS-R scores at 4,056 m were not significantly different between the MAR and LAR groups (Table 7). However, as noted earlier, 9 LAR subjects but only 1 MAR subject had symptom scores consistent with the presence of AMS. The wider range of AMS-C scores in the LAR group is illustrated in Figure 5. Fatigue scores between the two groups showed a significant ($p=0.049$) difference, with the MAR group having a lower fatigue score. However, there was no difference in alertness scores between the two groups (Table 7).

Figure 5. Frequency distribution histogram of AMS-Cerebral scores for both MAR and LAR groups at 4,056 m.



DISCUSSION

The key findings from this study follow: (1) MAR residing at ~2,000 m for greater than 90 days are mildly hypoxic at their residence altitude, (2) above 2,438 m, the MAR group resting SaO_2 was higher than the LAR group, (3) with increasing altitude, the range of resting SaO_2 widened more in the LAR group than in the MAR group, (4) for all subjects, the PETCO_2 at their residence altitudes showed an indirect correlation to PETO_2 and a direct correlation to PETCO_2 at 4,056 m, and (5) only 1 of the MAR subjects but 9 of the LAR subjects developed AMS during this brief ascent to 4,056 m. These findings are consistent with our hypothesis that lowlanders acclimatized to

moderate altitudes will maintain a higher level of arterial oxygenation when rapidly ascending to higher altitudes compared to lowlanders residing at low altitudes.

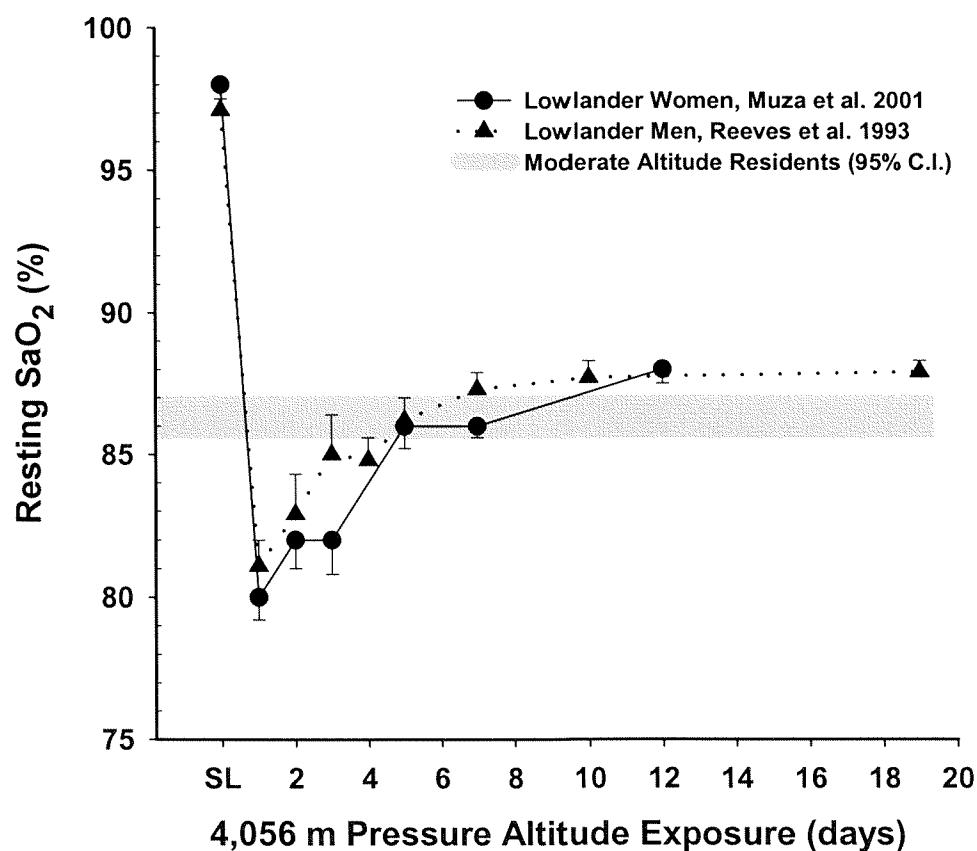
On one hand it is not a remarkable finding that individuals acclimatized to moderate high altitude (~2,000 m in this study) sustained a higher level of ventilation than unacclimatized lowlanders. However, this study provides the first quantitative assessment of the degree of ventilatory acclimatization achieved by a fit population residing at moderate altitudes. Thus, this work provides a quantitative basis for developing models and establishing guidelines for protecting Force health and sustaining operational performance during operations in high mountainous terrains.

Given the relatively large sample size used in this study, analysis of the dispersion of the ventilatory parameters measured was possible. The most significant finding was that the unacclimatized LAR subjects demonstrated a wider range of ventilatory responses to increasing high altitudes relative to the acclimatized MAR subjects (Fig. 2). This suggests that altitude acclimatization narrows the interindividual differences within a given population. Review of ventilatory data published from previous studies (13,14) of lowlanders residing for 12 or more days at 4,056 m demonstrate a similar narrowing of the range of ventilatory responses as acclimatization develops. We suspect that this narrowing of interindividual differences is primarily achieved by raising the ventilatory responses of subjects with the smallest ventilatory response to acute hypoxia. The present study suggests that the level of ventilatory acclimatization achieved at moderate altitude was sufficient to narrow the interindividual ventilatory differences at higher altitudes. Thus, moderate altitude residence results in a more uniform level of ventilatory acclimatization within that population.

As noted, previous studies have reported a large variation among individuals in the degree of ventilatory acclimatization at high altitude (20,22). Reeves et al. (14) reported that the variability in the degree of ventilatory acclimatization at high altitude was related to the individual's sea level end-tidal PETCO₂. That is, the lower the individual's PETCO₂ at sea level, the greater their ventilation at high altitude. The current study extends this relationship to subjects residing at moderate altitude (Table 5). This relationship may be potentially useful in predicting an individual's ventilatory response and subsequent well-being to a future high-altitude exposure. However, measurement of PETCO₂ requires sensitive analyzers and respiratory measurement apparatus that do not lend themselves to widespread use. On the other hand, the simple noninvasive and portable measurement of SaO₂ by pulse oximetry may provide a measure of ventilatory acclimatization under the proper circumstances. Because of the shape of the oxyhemoglobin dissociation curve, separation of individuals with wide-ranging degrees of ventilatory acclimatization does not occur until the arterial PO₂ drops below 60 mmHg, or a corresponding SaO₂ of about 92% (10). In the present study, this range of SaO₂ was observed starting at 2,438 m and was very apparent at 3,048 m (Table 6). Thus, measurement of resting SaO₂ at altitudes of 2,438 m or more are predictive of resting SaO₂ at higher altitudes and may be a useful clinical tool for assessing ventilatory acclimatization in a field or operational setting.

This study was designed to make a direct comparison of ventilatory and symptom responses to high altitude between the MAR and LAR groups. What the study did not do was provide a comparison between the MAR group and a LAR group that had achieved full ventilatory acclimatization to 4,056 m. However, numerous studies have reported the ventilatory response on arrival and during residence on the summit of Pikes Peak (3,4,13,14,24). The results of two of these studies (13,14) and our current study are illustrated in Figure 6. When sea level residents rapidly ascend to a pressure altitude of 4,056 m, on arrival their PETCO_2 is $34.9 \pm 2.8 \text{ mmHg}$ and their SaO_2 is $81 \pm 5\%$. It takes 9 - 12 days of continuous residence at high altitude for the SaO_2 to rise to $88 \pm 2\%$. By comparison, upon rapid ascent to 4,056 m, the MAR subjects' resting SaO_2 was $86 \pm 2\%$. These data suggest that personnel residing at ~2,000 m elevation for more than 90 days have acquired a level of ventilatory acclimatization equivalent to residing at 4,056 m for 5 - 9 days.

Figure 6. Comparison of MAR group resting SaO_2 ($\bar{X} \pm 95\%$ confidence interval) to LAR subjects from two prior ventilatory acclimatization studies at 4,056 m.



In many individuals, the stress of the hypoxic environment causes physiological dysfunctions, which may be manifest in the form of several altitude illnesses including AMS. AMS is a syndrome that is characterized by headache, anorexia, nausea, vomiting, insomnia, lassitude, and malaise (16). The syndrome has great individual variation in susceptibility; however, the hypoxia-induced symptoms are most common in unacclimatized, low-altitude residents who rapidly ascend to terrestrial elevations exceeding 2,500 m. Between 2,000 to 4,000 m, the incidence and severity of AMS in unacclimatized individuals rapidly increases from ~20% to ~70% (16). In addition, the development of AMS appears to be promoted by engaging in physical activities at high altitude. The symptoms of AMS commonly appear within 4 to 24 h of exposure, and usually resolve after several days as acclimatization to hypoxia is achieved. AMS is usually self-limited, but may progress into high altitude cerebral edema (HACE) or high altitude pulmonary edema (HAPE), both of which are potentially life threatening (15).

There is evidence that AMS-susceptible subjects have a relatively greater degree of hypoxemia compared to well subjects at high altitude. Many studies have reported that compared to well subjects, subjects who will develop and who have developed AMS have either a lower alveolar ventilation, alveolar oxygen partial pressure (PAO_2) or arterial oxygen saturation (SaO_2), or higher alveolar carbon dioxide partial pressure (PACO_2) (1,6,8,11,12,17,21). Although two recent studies (9,18) did not find significant differences in ventilation or SaO_2 between sick and well subjects at high altitude, the balance of data suggests a relatively greater hypoxemia in AMS-susceptible subjects compared to non-susceptible subjects at high altitude.

Given the degree of ventilatory acclimatization achieved by the MAR group, we would expect such personnel to be less susceptible to AMS. Our results are consistent with this view. Only one subject in the MAR group developed AMS, whereas nine subjects in the LAR group did. On the other hand, given the relatively short duration of high altitude exposure in this study, the approximately 23% incidence of AMS in the LAR group is higher than the literature would suggest (16). It is possible that early development of AMS is common and that previous studies have missed this early emergence of AMS symptoms simply because they did not assess AMS within this timeframe. Over the course of 24 - 49 h exposures to 4,056 m, AMS incidence is approximately 70% in unacclimatized lowlanders (16). Although the low incidence of AMS in the MAR group is predicted, because of the short exposure duration, we cannot discount the possibility that more members of the MAR group would develop AMS had the exposure duration been longer. However, we would predict a lower incidence of AMS in the MAR group compared to the LAR group at any length of high altitude exposure.

CONCLUSIONS

The results of this study support our hypothesis that lowlanders acclimatized to moderate altitudes will maintain a higher level of arterial oxygenation when rapidly ascending to higher altitudes compared to lowlanders residing at low altitudes. These data suggest that personnel residing at ~2,000 m elevation for more than 90 days have

acquired a level of ventilatory acclimatization equivalent to residing at 4,056 m for 5 – 9 days. The results also suggest that measurement of resting SaO_2 at altitudes of 2,438 m or more are predictive of resting SaO_2 at higher altitudes and may be a useful clinical tool for assessing ventilatory acclimatization in a field or operational setting.

Finally, we speculate that given the degree of ventilatory acclimatization achieved by personnel residing at the moderate altitude studied, we would expect such personnel to be less susceptible to high altitude sickness and decrements in cognitive and physical performance during rapid ascent to higher altitudes. Lowlanders who have achieved the level of acclimatization seen in our MAR group usually have complete restoration of cognitive performance and substantial improvements in physical work performance (2,25). However, quantitative assessment of the effects of moderate altitude residence on cognitive and physical work performance will require further studies. Nevertheless, the results of the present study suggest that military personnel residing at moderate altitudes for a period of at least 90 days can be rapidly deployed to higher altitudes of up to 4,056 m with a low probability of developing AMS and experiencing significant performance decrements.

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